

## **REMARKS**

### **Status of the Claims**

Claims 1-15 and 17-31 are pending in the application.

Claims 9, 14 and 18-31 have been withdrawn from consideration pursuant to 37 C.F.R. §1.142(b).

Claims 1-8, 10-13, 15 and 17 are currently under consideration with entry of this Response.

### **Summary**

Claims 1-15 and 17-31 are pending in the application, and claims 1-8, 10-13, 15 and 17 were examined in the Office Action dated 27 August 2009. Applicants note with appreciation that the rejection of claims 1-8, 10-13, 15 and 17 under 35 U.S.C. §112, first paragraph, has been withdrawn. However, the following claim rejections have either been maintained or are newly raised by the Office: **(a)** claims 1-8, 10-13, 15 and 17 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 30-37 of copending Application No. 11/183,477 ("the '477 Application"); and **(b)** claims 1-8, 10-13, 15 and 17 stand rejected under 35 U.S.C. §103(a) as unpatentable over International Publication No. WO 00/45790 to Berry et al. ("Berry") and U.S. Patent Publication No. US 2003/0180364 to Chen et al. ("Chen") in combination alone or further in view of Kasraian et al. (1999) Pharm. Dev. and Tech 4(4):475-480 ("Kasraian") and U.S. Patent Publication No. US 2002/0064536 to Hunt ("Hunt"). Applicants respectfully traverse all pending claim rejections for the following reasons.

### **The Obvious-Type Double Patenting Rejection**

Claims 1-8, 10-13, 15 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 30-37 of the '477 Application.

As noted at Page 3 of the Office Action, a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with the instant application.

Both the instant application and co-pending U.S. Patent Application No. 11/183,477 are commonly owned by DURECT Corporation as demonstrated in the Statements Under 37 C.F.R. §3.73(b). Accordingly, applicants have submitted herewith an executed Terminal Disclaimer to Obviate a Provisional Double Patent Rejection Over a Pending “Reference” Application, along with the subject accompanying Statement Under 37 C.F.R. §3.73(b) in compliance with 37 CFR §1.321(c).

Applicants respectfully submit that submission of the Terminal Disclaimer is fully responsive to the Provisional Obviousness-Type Double Patenting rejection over co-pending U.S. Patent Application No. 11/183,477. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

#### The Rejection under 35 U.S.C. §103

Claims 1-8, 10-13, 15 and 17 stand rejected under 35 U.S.C. §103(a) as unpatentable over Berry and Chen, in combination alone or further in view of Kasraian and Hunt. Applicants respectfully traverse the rejection for the following reasons.

In pertinent part, 35 U.S.C. §103 provides that a patent may not be obtained “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art.” 35 U.S.C. §103. Any analysis under Section 103 must consider the following factual inquiries: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness (such as commercial success and long-felt but unsolved need, failure of others, and unexpected results). *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, (1966) (the “*Graham* factors”). The Supreme Court, in *KSR Intern. Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007) reaffirmed that the *Graham* factors “continue to define the inquiry that controls” an obviousness

analysis. Furthermore, when considering the above-noted Graham factors, the Office must adhere to the following rules: (a) the claimed invention must be considered as a whole; (b) the references must be considered as a whole; (c) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (d) reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

(A) The claimed invention must be considered as a whole.

Applicants have disclosed and claimed a unique set of pharmaceutical formulation chemistries that provide unexpected and beneficial performance characteristics. More particularly, applicants have found that a stable nonaqueous drug formulation can be obtained (stable at elevated temperatures for at least 2 months) when the polymer component is pre-treated with methionine in an amount sufficient to reduce vehicle peroxide values below 5 ppm.

(B) The Primary (Berry) reference must be considered as a whole.

The Office has continued to misconstrue the Berry reference. Berry describes a problem seen with prior lipid vehicle systems (presence of peroxides). Berry then offers a solution to this problem by teaching that their polymer compositions should be used instead – i.e., their polymers DO NOT CONTAIN peroxides and are therefore better than using the lipid system that would contain peroxides.

Accordingly, when Berry is considered as a whole (as required under Section 103), it is clear that Berry believed that the use of their polymer formulations would avoid peroxide problems – i.e., Berry believed that use of their polymer formulations would avoid peroxide problems as seen with prior lipid vehicle formulations. In other words, the Office's primary reference used to support its' conclusion of obviousness actually teaches that polymer compositions would not present peroxide problems.

(1) Berry does not disclose applicants' recited formulations;

The Office has acknowledged that Berry does not teach applicants' recited formulations (solvent nor active agent). Office Action at page 7, first full paragraph.

(2) None of the Secondary References disclose applicants' recited formulations;

Chen does not teach applicants' recited formulations (Chen fails to even mention peroxides, suggesting to the skilled person that again, the polymer compositions taught by Chen would not be subject to a peroxide contamination problem). Accordingly, when the Office's proposed combination of Berry and Chen is considered as a whole for what the two references fairly teach the skilled person – one finds that use of polymer systems would avoid the peroxide problems seen with liposomes (Berry), and that a number of polymer systems can be usefully developed and used without having any reported problems with peroxide contamination (Chen).

Kasraian does not teach applicants' recited formulations (Kasraian merely identified peroxide content in a PVP excipient, and then taught that one should add an antioxidant to their pharmaceutical formulation -- and thus NOT REMOVE PEROXIDES from the PVP excipient).

Hunt does not teach applicants' recited formulations (Hunt merely teaches use of oxidative sinks -- and thus NOT REMOVAL OF PEROXIDES).

Accordingly, when the cited art (the combination of Berry, Chen, Kasraian and Hunt) is considered as a whole (as required under Section 103), it is clear that the art fails to disclose applicants' recited formulations.

(C) The Office has construed prior art using impermissible hindsight vision afforded by the claimed invention.

At page 15 of the Office Action, the Office confirms that it must use hindsight reasoning in order to piece the bits and pieces of prior art together and arrive at applicants' invention. The Office states that this is OK if it only takes into account information from the prior art and not knowledge gleaned from applicants' specification. However, applicants note that the only way to arrive at applicants' invention from the cited references is through the knowledge provided by applicants' specification. The Office's primary reference teaches exactly away from the presence of peroxides in Berry's polymer systems. The primary reference does not contain two of the recited elements of applicants' formulation (Berry's formulation does not contain BA or interferon). The Office has taken the position that solvents are independent and distinct from other solvents, that is, they are each patently distinct species, and further that interferons are independent and distinct from other drugs, that is, interferons are patently distinct species from other drugs. See Species Election Requirement from Office Action dated 28 June 2007. Accordingly, not only does Berry teach away from applicants' invention, Berry's solvent and drug combination from Berry are patentably distinct from applicants' solvent and drug combination.

In order to meet its burden in establishing a rejection under 35 U.S.C. §103 the Office must first demonstrate that the cited art teaches or suggests all the claimed limitations. *See Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007). Furthermore, as indicated by the Supreme Court in *KSR Int'l Co. v. Teleflex Inc.*, in order to avoid pitfalls such as impermissible hindsight reconstruction, it will often be necessary "to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007).

The only possible way to navigate the course for the Office's picking and choosing from the cited references is to use applicants' specification as a road-map in an impermissible hindsight reconstruction of applicants' recited invention. In such cases, where one can only "vary all parameters or try each of numerous possible choices until

one possibly arrive[s] at a successful result, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful” (*In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988), the finder of fact “should not succumb to hindsight claims of obviousness.” *In re Kubin*, \_\_ F.3d \_\_, No. 2008-1184, slip op. at 14 (Fed. Cir. 2009).

(D) The Office has failed to show that there would have been a reasonable expectation of success for applicants’ recited formulations.

Since the Office’s proposed reconstruction of the cited references must ignore the plain teachings provided by those references, there cannot have been a reasonable expectation of success for applicants’ invention.

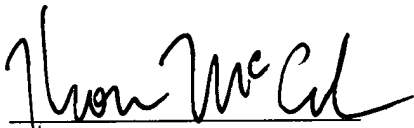
Accordingly, contrary to the Office’s assertions, the proposed combination of Berry and Chen in further view of Kasraian and Hunt fails to establish a showing of *prima facie* obviousness. Reconsideration and withdrawal of the rejection of claims 1-8, 10-13, 15 and 17 under 35 U.S.C. §103(a) is thus earnestly solicited.

**CONCLUSION**

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

The appropriate fee is either attached or authorized. If the Commissioner determines that an additional fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953**.

Respectfully submitted,



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